Appeal No. 2012-1490, -1508

UNITED STATES COURT OF APPEALS

for the

FEDERAL CIRCUIT

BUTAMAX(TM) ADVANCED BIOFUELS LLC,
Plaintiff/Counterclaim Defendant-Appellant,

and

E.I. DUPONT DE NEMOURS AND CO.,
Counterclaim Defendant,

– v. –

GEVO, INC.,
Defendant/Counterclaimant-Cross-Appellant

Appeal from the United States District Court for the District of Delaware
in Case No. 11-CV-0054, Judge Sue L. Robinson

NON-CONFIDENTIAL OPPOSITION BRIEF FOR DEFENDANT/COUNTERCLAIMANT-CROSS-APPELLANT GEVO, INC.

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August 17, 2012

CERTIFICATE OF INTEREST

Pursuant to Fed. Cir. R. 26.1, 28(a)(1), and 47.4, counsel for Defendant/Counterclaimant-Cross Appellant Gevo, Inc., certifies the following:

1. The full name of every party represented by me is:

   Gevo, Inc.

2. The names of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

   N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the parties represented by me are:

   N/A

4. The names of all law firms and partners or associates that appeared for the parties now represented by me in the trial court or are expected to appear in this Court are:

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CONFIDENTIAL MATERIAL OMITTED

Confidential material has been omitted from this Opposition Brief. Such confidential information relates to the parties's research and development, business and financial information subject to protection pursuant to the district court's Protective Order.

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PRELIMINARY STATEMENT

After carefully considering multiple rounds of written submissions, and conducting a two-day hearing with live witnesses and video testimony, the district court issued a well-reasoned 25-page opinion explaining in detail why Butamax is not entitled to the extraordinary relief of a preliminary injunction. As made plain in the district court's opinion, Butamax's application for a preliminary injunction was not a close call. The evidence presented led the district court to conclude that Butamax likely "does not hold a valid patent, nor would [Gevo] infringe if it did."[1]

On appeal, Butamax bears a heavy burden. Butamax must show the district court abused the wide discretion afforded to the lower courts in deciding preliminary injunction motions. Butamax's burden is especially heavy because it seeks to reverse the denial of a preliminary injunction, which held against it on both infringement and validity.[2] Butamax fails to advance any compelling argument to meet its burden. Instead, Butamax rehashes the same unconvincing arguments that led this Court to stay the district court's injunction pending this appeal by finding that Gevo has a strong likelihood of success on the merits or that

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[1] (PI Order A2-A27 at A26.)

[2] *Altana Pharma AG v. Teva Pharms. USA, Inc.*, 566 F.3d 999, 1005 (Fed. Cir. 2009).

it has demonstrated a substantial case and that the harm factors militate in its favor.[3]

As set forth on pages 14 to 19 of its principal brief, Butamax's assertions of error rely extensively, if not solely, on the interpretations and conclusions advanced by its experts as if they constitute the "undisputed truth." The district court, however, considered the testimony of Butamax's experts and made its credibility determinations and findings on the merits of Butamax's motion. To put it simply, Butamax ignores the district court's careful consideration of the extensive record before it and attempts to *manufacture* error where there is none.

For example, Butamax asserts that the district court found explicit anticipation based on Larroy I.[4] Not so. The district court found that one element – isobutanol production – was explicitly disclosed and that Larroy I, as well several other references, inherently anticipate Butamax's patent.[5] Similarly, Butamax alleges that the district court relied only on Larroy I to find anticipation of claim 14, when it was not alleged to be anticipatory. The district court,

[3] (D.I. 47.)

[4] (BM Br. at 53.)

[5] (PI Order at A22-23.)

however, concluded that several other prior art references independently anticipated that claim.[6]

Further, Butamax asserts that Gevo's experts allegedly made "admissions" that support Butamax's contentions. Here again, Butamax ignores the fact that the district court considered all of the evidence before it, including the same out of context "admissions" cited by Butamax, and concluded that Butamax likely "does not hold a valid patent, nor would [Gevo] infringe if it did." As explained more fully below, this Court should affirm the district court's denial of Butamax's motion for preliminary injunction.

[6] (*Id.*)

COUNTER-STATEMENT OF THE ISSUES[*]

1. Whether the district court abused its discretion on the issues of non-infringement and invalidity such that a remand is warranted:
    a. Was it an abuse of discretion to find the claim limitation "acetohydroxy acid isomeroreductase enzyme" is defined in the patent's specification?
    b. Was it an abuse of discretion to find Gevo likely did not infringe under any reasonable claim construction?
    c. Was it an abuse of discretion to find Gevo raised a substantial question of validity and Butamax is unlikely to succeed on the merits?
    d. Was it an abuse of discretion to find Butamax claimed a natural and known pathway of isobutanol production and the minor modification that Butamax made to it is also disclosed in the prior art?
    e. Was it an abuse of discretion to find claim 13 of Butamax's patent likely failed to meet the statutory requirements for written description and enablement?
2. Whether the district court abused its discretion on the issue of irreparable harm where Butamax's alleged damages can be calculated and the balance of equities and public interest favors Gevo?

[*] In light of this Court's decision granting a stay of the district court's injunction pending appeal, Gevo's cross appeal (No. 2012-1508) is now moot. (D.I. 47.)

COUNTER-STATEMENT OF THE FACTS

The district court's well-reasoned opinion is the result of careful consideration of the evidence before it. After Butamax filed its motion for preliminary injunction, the district court granted both parties the opportunity to take extensive discovery specifically for the preliminary injunction. This included 13 depositions, 10 witness declarations, and hundreds of exhibits (including over 200 exhibits filed by Butamax alone). The parties also submitted a full round of briefing prior to a two-day evidentiary hearing. During the hearing, the district court observed live and video-recorded witnesses. Subsequent to the hearing, the parties made additional submissions to the district court, and the district court issued its opinion after more than three months of considering the evidence. The district court found that Butamax was unlikely to prevail at trial. Additionally, on a preliminary review of the same arguments advanced by Butamax, this Court found that Gevo was likely to prevail on appeal. (D.I. 47.)

I. BUTAMAX'S ATTEMPTS TO CAPTURE SUBJECT MATTER BEYOND THE SCOPE OF ITS PATENT

A. NADPH-Dependent Versus NADH-Dependent KARI Enzymes

The production of isobutanol proceeds naturally through a series of enzymes, one of which is known as a KARI ("acetohydroxy acid isomeroreductase") enzyme. The difference between a KARI enzyme that is

NAD**P**H-dependent and one that is NADH-dependent is substantial. At the time Butamax filed its patent application and to this day, all known KARI enzymes found in nature are NAD**P**H-dependent. Within a yeast cell, NADH and NAD**P**H, while structurally similar, "*are not metabolically interchangeable.*" (Voet, Biochem. at 892 (emphasis in original), A8780, A8783.) Gevo's creation of an NADH-dependent KARI enzyme is critical to high-yield production of isobutanol because very little NAD**P**H is present under fermentation conditions.

The difference between the NADH-dependent pathway that Gevo uses and those claimed in Butamax's patent, U.S. Patent No. 7,993,889 ("the '889 patent") creates a substantial difference in the final yield for producing isobutanol.

[redacted]

B. The '889 Patent's KARI Is Defined To Exclude An NADH-Dependent KARI

The district court recognized that Butamax's patents did not include Gevo's NADH-dependent KARI. Specifically, the district court twice rejected the argument that Butamax presents again on appeal — that the claim limitation "acetohydroxy acid isomeroreductase" should be given its "ordinary meaning" despite having been expressly defined in the specification:

> The patent contains a definitions section and explains that the "following definitions . . . are to be used for the interpretation of the claims and the specification." Accordingly, the court interprets the term acetohydroxy acid isomeroreductase in the manner in which [Butamax] defined it, namely, as an enzyme that is solely NADPH-dependent (as opposed to NADH-dependent or NADH and NADPH-dependent).

((PI Order, A11-12; A14 n.7 (citations omitted; emphasis added).) The district court found that this interpretation was supported by the remainder of the specification because while Butamax argued the meaning of the term was "an enzyme that utilizes NADPH ***and/or*** NADH," this could not be the case because "other enzymes in the patent are specifically identified as using 'NADH ***and/or*** **NADPH** ***as an electron donor***.'" (*Id.* at A12 (emphasis added).)

The district court reasoned that "because [Butamax] . . . knew how to define a term by reference to an NADH cofactor, the term acetohydroxy acid isomeroreductase is properly construed as excluding an enzyme that is in any way NADH dependent." (*Id*. at A13.) Although the district court acknowledged that some negligible NAD**P**H activity might exist in the system, it determined that Gevo did not infringe because by defining "the KARI as exclusively NADPH-dependent, [Butamax] has placed [Gevo]'s use of an NADH-dependent, or primarily NADH-dependent enzyme, outside the scope of claim 1." (*Id*. at A14.)

1. Butamax's '889 Patent's KARI Includes Only The Use Of NADPH

Butamax's patent is directed generally to a natural five-step process of converting pyruvate to isobutanol. Each of those claimed steps is mediated by a different enzyme, and Butamax explicitly defined many of those enzymes. ('889 patent, 325:16-43, A78, A83-86, A243.)

While Butamax argued intensely below (and now on appeal) for a plain meaning construction, the patentee included a specific definition for the term. The '889 patent states that "[t]he following definitions . . . are to be used for the interpretation of the claims and the specification." ('889 patent, 6:52-53, A83.) Four columns of definitions follow. Each uses offsetting quotes and explains what the term "herein" refers to. The term at issue, "acetohydroxy acid isomeroreductase" (KARI) is the fourth definition and uses quotes to define the term:

> The terms "acetohydroxy acid isomeroreductase" and "acetohydroxy acid reductoisomerase" are used interchangeably herein to refer to an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate ***using NADPH*** . . . as an electron donor.

('889 patent, 7:8-13, A84 (emphasis added).) Other enzymes, however, allowed the use of either NADH or NAD**P**H. For example:

> The term "acylating aldehyde dehydrogenase" refers to an enzyme that catalyzes the conversion of isobutyryl-CoA to

> isobutyraldehyde, ***using either NADH or NADPH*** as electron donor.

(*Id.* at 8:17-20, A84 (emphasis added).) Butamax's ability to identify both cofactors contained even another iteration, where another enzyme "utilize[d] NADH . . . ***and/or*** NAD**P**H" as an electron donor." (*Id.* at 7:54-56, A84.)

2. Butamax's Infringement Expert Ignores The '889 Patent's Lexicography

Butamax's witness, Dr. Patricia Babbitt testified to plain meaning (*see* PI Tr. at 217:14-219:13, 224:21-23, 226:4-24, A16516, A16570-73) even though she agreed that the definition of the term "acetohydroxy acid isomeroreductase" appeared in the definitions section of the patent:

> Q. And you don't disagree that this term appears in the definition section of this patent; right?
>
> A. I don't disagree with that.

(PI Tr. at 232:9-11, A16574.) She nonetheless went on to insist that the patent did not define the enzyme:

> Q. Now that says . . . . "the terms acetohydroxy acid isomeroreductase, and acetohydroxy acid reductoisomerase." Those would be KARIs; right?
>
> A. Yes.
>
> Q. Are used interchangeably herein to refer to an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxy isovalerate using NADPH reduced nicotinamide . . . as an electron donor; is that right?

> A. That's what it says.
>
> Q. And so that would be a definition that's provided in the '889 patent following this statement that says that when interpreting these claims, you are to use these definitions; right?
>
> A. That's not how the enzyme listed there is defined formally.
>
> Q. Right. But the patent here, you'll agree with me, says, we're supposed to use these definitions; right?
>
> A. I don't consider that a ***definition***. I considered it a ***descriptor***.

(PI Tr. at 229:8-231:2, A16573-74 (emphasis added).) Indeed, Dr. Babbitt did not provide any testimony interpreting the definition in the patent specification, which she acknowledged is different from how the enzyme "is defined formally." (*Id.* at 230:18-23, A16574.)

3. After Butamax Realized NADH-Dependent Enzymes Could Be Made It Included Them In A Different And Subsequent Patent Application

Butamax had not considered NADH-dependent KARI enzymes at the time it filed its provisional patent application, and only changed its definition of a KARI to include NADH-dependent variants in 2008. [redacted]

[redacted]

Butamax waited until 2008 to include an NADH-dependent KARI in a patent application. That application professed that the allegedly novel element of the alleged invention was the KARI's ***use*** of NADH:

> DETAILED DESCRIPTION OF THE INVENTION
>
> **[0054]** The present invention relates to the generation of mutated KARI enzymes to use NADH as opposed to NADPH. These co-factor switched enzymes function more effectively in microbial systems designed to produce isobutanol.

(U.S. 12/337,736 at ¶ 54, A6276, A6392-96 at A6296.) The application further stated that NADH-binding enzymes did not even previously exist:

> **[0006]** While methods described above indicate the potential of isobutanol production via biological means these methods are cost prohibitive for industrial scale isobutanol production. The biosynthesis of isobutanol directly from sugars would be economically viable and would represent an advance in the art. However, to date the only ketol-acid reductoisomerase (KARI) enzymes known are those that bind NADPH in its native form, reducing the energy efficiency of the pathway. A KARI that would bind NADH would be beneficial and enhance the productivity of the isobutanol biosynthetic pathway by capitalizing on the NADH produced by the existing glycolytic and other metabolic pathways in most commonly used microbial cells. The discovery of a KARI enzyme that can use NADH as a cofactor as opposed to NADPH would be an advance in the art.

(U.S. 12/337,736 at ¶ 6, A6292.) The application also acknowledged that cofactor switching to create an NADH-dependent enzyme would greatly enhance its

effectiveness but to do so successfully would be "unpredictable." (*Id.* at ¶ 9, A6292.)

Two years later, in December of 2010, but nearly a year before the issuance of the '889 patent, Butamax filed a continuation-in-part ("CIP") patent application related to the '889 patent family where it changed the very definition of the KARI enzyme at issue by stating the enzymes in the CIP application "use electron donors ***such as NADPH and/or NADH*** for the conversion of acetolactate to 2,3-dihydroxy-isovalerate," and added several described sequences. (U.S. 12/966,333 at ¶ 55, A6235, A6241 (emphasis added).) That application further discloses numerous additional sequences that were not present in Butamax's original application. (*Id.* at ¶¶ 55, 96-97, A6241, A6245-46.)

II. THE DISTRICT COURT CREDITED DR. KIRSCH'S TESTIMONY THAT GEVO DOES NOT INFRINGE

The district court considered the video-taped testimony and declaration of Dr. Jack Kirsch, a professor of biochemistry, biophysics and structural biology at the University of California at Berkeley. (Kirsch Decl. at ¶¶ 18-42, A7214-25.)

Dr. Kirsch explained that enzymes are defined by the chemical reactions that they catalyze. Within a yeast cell, NADH and NAD**P**H, while structurally similar, "*are not metabolically interchangeable.*" (Voet, Biochem. at

892 (emphasis in original), A8783.) This is because they are involved in fundamentally different parts of the yeast metabolism. The NAD form of NAD(H) is generally employed in breaking down large molecules into smaller ones. (Kirsch Decl. ¶ 31, A7219, Voet, Biochem. at 892, A8783; *see also* Carugo at A8785.) It is very uncommon for NAD**P**H to be employed for this purpose. NAD**P**H is employed in assembling small molecules into larger ones. (Kirsch Decl. ¶ 31, A7219.)

Dr. Kirsch also testified that, from the perspective of one of skill in the art, the use of a single cofactor, NAD**P**H, as an electron donor in the definition demonstrated that only NAD**P**H-dependent enzymes were contemplated by the claims. (*Id.* at ¶¶ 19-21, A7215-16.) Thus, KARI and other enzymes, are defined by the co-factors and substrates that they catalyze. For this reason, the international authority charged with classifying such enzymes often classifies enzymes dependent on NADH differently than those dependent on NAD**P**H. (Kirsch Decl. ¶¶ 28-29 and n.6, A7218-19; Kirsch Ex. G, IUB-Recommendations at 5 and 29, 34-35, 38, 42, 47, A8770-78.) In other words, the enzymes are categorized by the co-factor that they primarily use, even if they contain some, or even significant activity in the other cofactor. Further, Dr. Kirsch explained that the EC number 1.1.1.86 chosen by Butamax defined the enzymes as NAD**P**H dependent:

IUBMB Enzyme Nomenclature

EC 1.1.1.86

Accepted name: ketol-acid reductoisomerase

Reaction: (*R*)-2,3-dihydroxy-3-methylbutanoate + $NADP^+$ = (*S*)-2-hydroxy-2-methyl-3-oxobutanoate + NADPH + H^+

(Kirsch Decl. ¶ 34, A7220-21; Ex. G at 34, A8774.)

[redacted]

III. THE DISTRICT COURT FOUND THE '889 PATENT IS LIKELY INVALID

A. The District Court Correctly Determined Claims 1 And 14 Of The '889 Patent Are Likely Anticipated

Butamax's claim 1 sets forth a five-step pathway that leads from pyruvate to isobutanol where, as the district court found, one of the steps is engineered:

> A method for producing isobutanol comprising;
>
> a. providing a fermentation media comprising carbon substrate; and
>
> b. contacting said media with a recombinant yeast microorganism expressing an engineered isobutanol biosynthetic pathway wherein said pathway comprises the following substrate to product conversions;
>
> i. pyruvate to acetolactate (pathway step a);
>
> ii. acetolactate to 2,3-dihydroxyisovalerate (pathway step b);
>
> iii. 2,3-dihydroxyisovalerate to α-ketoisovalerate (pathway step c);
>
> iv. α-ketoisovalerate to isobutyraldehyde (pathway step d); and

---

(...continued)

[8] Dr. Glassner, Gevo's Executive Vice President of Technology, gave similar testimony. (PI Tr. at 359:18-360:7, A16613, A16642.)

> v. isobutyraldehyde to isobutanol (pathway step e);
>
> and wherein
>
> a) the substrate to product conversion of step (i) is performed by an acetolactate synthase enzyme;
>
> b) the substrate to product conversion of step (ii) is performed by an acetohydroxy acid isomeroreductase enzyme;
>
> c) the substrate to product conversion of step (iii) is performed by an acetohydroxy acid dehydratase enzyme;
>
> d) the substrate to product conversion of step (iv) is performed by a decarboxylase enzyme; and
>
> e) the substrate to product conversion of step (v) is performed by an alcohol dehydrogenase enzyme;
>
> whereby isobutanol is produced.

('889 patent, Claim 1, A243.) Claim 14 additionally requires that one of the enzymes "uses NADH as an electron donor." (*Id.*, Claim 14.)

The district court found that Gevo raised a substantial question that claims 1 and 14 are inherently anticipated and Gevo's "invalidity defenses do not lack substantial merit." (PI Order at A22.) The district court's fact-finding on inherent anticipation is simple – Butamax's claims are broad enough to cover a natural and well-known isobutanol pathway modified along any site in the pathway. (*Id.* at A17-24.) This finding is not only amply supported by the record, it is the same conclusion reached by the PTO during reexamination of Butamax's

patent. Indeed, as a result of this determination and the others summarized above, "the court has concluded that [Butamax] does not hold a valid patent, nor would [Gevo] infringe if it did . . . ." (*Id.* at A26.)

As a preliminary matter, contrary to Butamax's representation, the district court's opinion focused on inherent – and not express – anticipation. For example, the district court carefully noted that the reexamination examiner rejected the claims because natural yeast "converting pyruvate to isobutanol ***inherently*** possess the enzymes capable of carrying out the isobutanol synthetic pathway reactions found in claim 1." (*Id.* at A18 (emphasis added).) The district court also noted that "[Gevo's expert testified that] it was well known in the art that the 'anabolic pathway' recited in claim 1 of the '889 patent is inherently present in yeast; thus, the prior art references . . . are inherently anticipatory." (*Id.*) The district court ultimately concluded that the claims encompassed "the *inherent* reactions . . . disclosed in the prior art references related to claim 14." (*Id.* at A22 n.16 (emphasis added).)

Moreover, the district court rejected the opinions of Butamax's expert, Dr. Alexander Klibanov, who testified that an anticipating yeast would require the modification of all five of the pathway enzymes; instead the district court adopted a construction that required only a single part of the pathway to be modified to meet the limitations of claim 1. (*Id.* at A20-21.) Applying this claim construction,

which Butamax does not challenge on appeal, the district court held that ***several references*** each individually disclosed the claimed invention. (*Id.* at A21-22.) Thus, the district court held that Gevo's "invalidity defenses do not lack substantial merit" and indeed, raised "a substantial question regarding the validity." (*Id.* at A22.)

In so holding, the district court rejected Butamax's arguments with respect to claim 1 that none of the prior art yeast "disclose isobutanol production." (*Id.* at A22-23.) In addition to crediting Gevo and the reexamination examiner's analysis, the district court found that several prior art references disclose isobutanol production in engineered yeast. Among them, the district court found that Larroy I ***explicitly*** disclosed the isobutanol production required by the claim. (*Id.* at A21-23.) Consequently, given the natural isobutanol pathway, the explicit production of isobutanol in Larroy I, and the isobutanol production in the other references, the district court found inherent anticipation based on each of these references. (*Id.* at A22.)

In finding that the pathway claimed is a natural pathway in prior art yeast, the district court implicitly credited Dr. Stephanopoulos' explanation that the pathway set forth in the claims is a natural pathway mapped in the prior art and that one of these steps has been modified on several occasions. (*See, e.g.*, PI Tr. at 59:15-22, 60:6-74:12, 76:16-82:18, A16531-37.) Among others, the pathway is

present in the Aryapaa, Chen and Boulton references. (*Id.*) Dr. Stephanopoulos testified that, as demonstrated in the Chen paper, this was the primary isobutanol pathway in yeast. (PI Tr. at 67:10-74:12, A16533-35.)

For example, the Boulton reference shows the claimed pathway in figure 3.14:

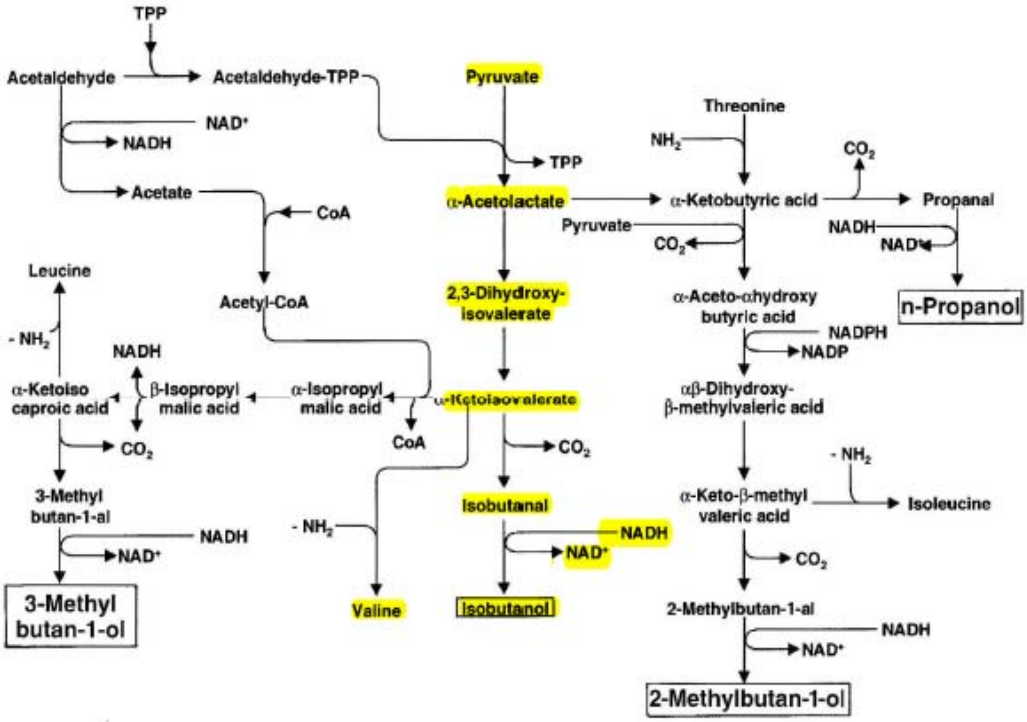


Fig. 3.14 Biosynthetic routes for synthesis of some higher alcohols important to beer flavour and aroma.

(Steph. Decl. at ¶ 10, A9805-31 at A9810-12; Steph. Ex. 8, Boulton, A9962, A9980 (emphasis added).) Adjusting for slight differences in terminology, the figure demonstrates that this natural pathway proceeds through the same steps as the patented method:

i. Pyruvate to α-acetolactate (*i.e.*, acetolactate);

ii. α-acetolactate (*i.e.*, acetolactate) to 2,3-dihydroxyisovalerate;

iii. 2,3-dihydroxyisovalerate to α-ketoisovalerate;

iv. α-ketoisovalerate to isobutanal (*i.e.* isobutyraldehyde); and

v. isobutanal (*i.e.* isobutyraldehyde) to isobutanol.

(Steph. Decl. ¶ 10, A9810-12.)

Boulton further discloses that this reaction is mediated by the claimed enzymes. Butamax's expert, Dr. Klibanov, agreed that each of these enzymes was disclosed in the reference. (PI Tr. at 300:2-302:21, A16627-28.) First, Boulton explained in a figure that ***all*** of the higher alcohols (including isobutanol) use the claimed enzymes for steps iv and v:

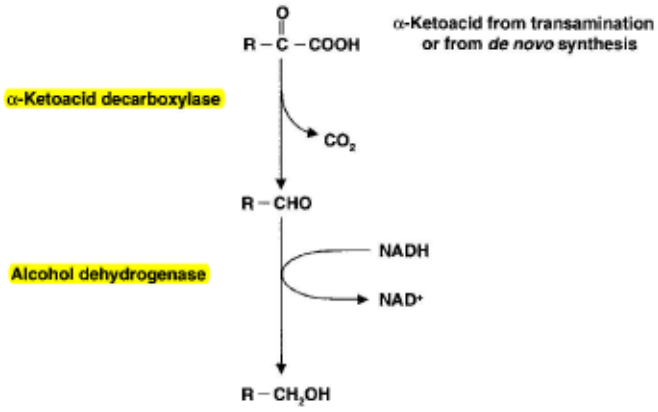
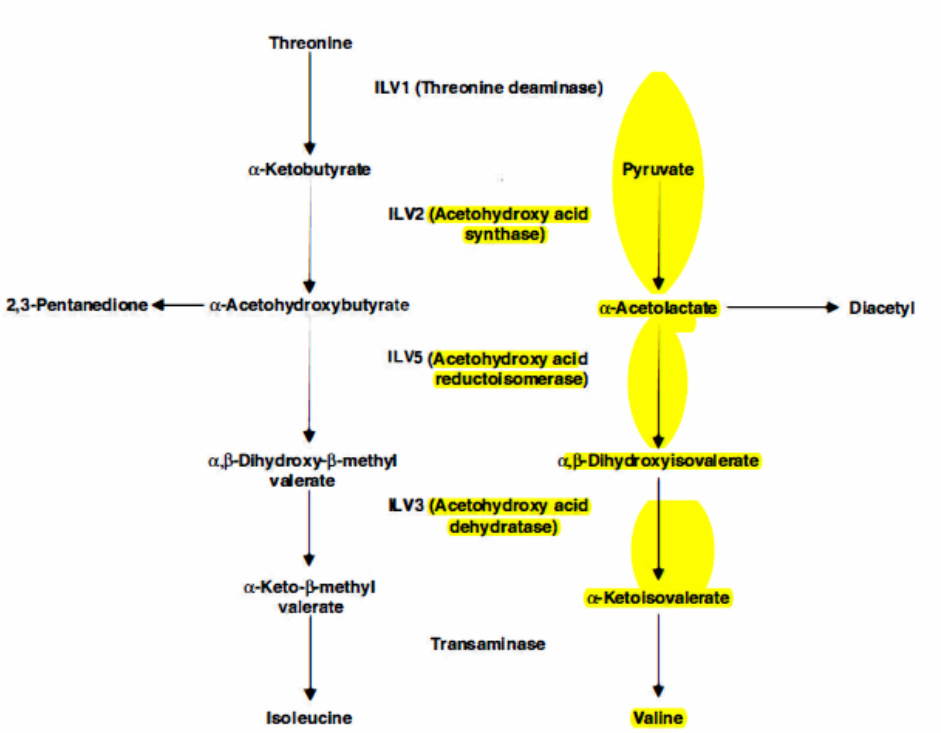


Fig. 3.13 Generalised scheme for higher alcohol synthesis.

(Steph. Decl. ¶ 16, A9815-16; Steph. Ex. 8, Boulton, A9978-79 (emphasis added).) Second, in its discussion of the valine pathway, which shared its first three steps with the isobutanol pathway, Boulton showed the first three claimed enzymes:



(*See* Steph. Ex. 8, Boulton, A9997, A9980 (emphasis added).) Dr. Stephanopoulos explained that these are the same enzymes and occur in the same order as the enzymes in claim 1. (Steph. Decl. ¶¶ 12-14, A9813-14.)

Dr. Stephanopoulos also presented a series of references, including Yocum and Larroy I, where one of the enzymes of the claims was modified. (Steph. Decl. ¶¶ 20-31, A9818-23.) One of those references, Larroy I, mapped the same pathway from pyruvate to isobutanol and, as the district court found, expressly disclosed isobutanol production. (Steph. Decl. ¶ 22, A9819; *see also* A10087, A10094-95.)

Because the last enzyme – the non-KARI enzyme – is naturally NADH-dependent (as shown in the Boulton pathway above), Dr. Stephanopoulos

testified that Claim 14 was also inherently anticipated. (PI Tr. at 58:24-60:16, 80:14-81:20, A16531, A16536.)

B. The District Court Correctly Found The '889 Patent Likely Does Not Disclose Or Enable The "PDC Knockout"

The district court concluded that Gevo "raised a substantial question as to whether the specification of the '889 patent provides a sufficient written description of claim 13" and "whether claim 13 is enabled." (PI Order at A24.) With respect to written description, the district court recognized that it was undisputed that there was no explicit disclosure of a PDC ("pyruvate decarboxylase") knockout in the specification. (PI Order at A23 (finding that "there is no dispute that the specification of the '889 patent does not specifically disclose the requirement of 'inactivated genes'" that "reduce pyruvate decarboxylase activity").) Butamax's expert, Dr. Klibanov, admitted that the four corners of the '889 patent do "[n]ot specifically" disclose the limitations of claim 13, including the PDC knockout limitation. (PI Tr. at 291:11, A16625.) Similarly, Gevo's expert, Dr. Stephanopoulos, "went through all of the 50 columns of the ['889] specification . . . looking for a place where there is a written description for the – the knock out of this pyruvate carboxylase enzyme and there is no place where there is evidence of that, or written description of anything related to that." (PI Tr. at 87:7-12, A16538.)

Butamax nonetheless picked three unrelated portions of the specification in an attempt to satisfy the written description requirement. The district court considered and rejected each of Butamax's arguments. (PI Order at A23-24.) Butamax cited to column 12 of the '889 patent. In addressing this section, Gevo's expert Dr. Stephanopoulos testified that the section "is not even about pyruvate decarboxylase . . . [it] is about decarboxylation of another key molecule . . . α-KIV." (PI Tr. at 89:6-9, A16538.) Even Dr. Klibanov admitted that this citation "does not talk about . . . genes," or disclose inactivating genes to reduce PDC activity. (PI Tr. at 287:17, A16624.) After considering all of this testimony, the district court found that the citation provides "no discussion about gene inactivation or about PDC in [an inactivation] context." (PI Order at A23.)

Butamax also relied upon a citation of Dickinson, which appears in the Background section of the '889 patent, along with several other references. ('889 patent, 1:46-47, A81.) Dr. Stephanopoulos testified that the single paragraph where Dickinson is cited "is not related to the decarboxylation of pyruvate" but instead deals "with the iso-ketoisovalerate because it is talking about ketoacid decarboxylation," which is from the Ehrlich pathway. (PI Tr. at 91:20-92:1, A16539; PI Order at A24.) Consistent with Dr. Stephanopoulos, Dr. Klibanov admitted that this citation does not state anything about inactivating PDC genes. (PI Tr. at 290:1, A16626.) Further, as Dr. Klibanov admitted, the citation does not

provide any reason for visiting Dickinson, "[i]t just gives a reference." (PI Tr. at 290:5, A16626.) After considering this testimony, the district court concluded that Dickinson cannot be used to provide § 112 support because it "is neither incorporated by reference, nor is it cited in the '889 patent in the context of deleting PDC genes." (PI Order at A24.)

Butamax also pointed to the general statement that "[t]he microbial host . . . has to be manipulated in order to inactivate competing pathways for carbon flow by deleting various genes." ('889 patent, 16:55-57, A88.) Dr. Stephanopoulos again explained that this generic statement has "nothing to do with pyruvate carboxylase [PDC]" because it provides "no mention of which genes, which competing pathway, [or] which deletion" would be required. (PI Tr. at 91:8-14, A16539.) Dr. Klibanov agreed that the citation did not specify inactivating genes that reduce PDC activity. (PI Tr. at 289:1-3, A16624.) After weighing the credibility of the expert witnesses, the district court concluded that a "generic suggestion to inactivate competing pathways does not teach anything specific about reducing PDC activity by inactivating those genes." (PI Order at A24.)

With respect to enablement, the parties' experts disagreed as to the "extent of experimentation it would take to create the PDC-knock out isobutanol-producing yeast of claim 13." (PI Order at A24.) After carefully considering the credibility of witnesses presented by both sides, the district court found that there

is a substantial question regarding whether claim 13 is enabled. (*Id*.) [redacted]

[redacted]

IV. BUTAMAX OVERSTATES THE DISTRICT COURT'S FINDINGS ON IRREPARABLE HARM AND BALANCING THE EQUITIES

The district court stated that its "finding of invalidity and noninfringement effectively ends the preliminary injunction analysis." (PI Order, A22.) The district court, however, briefly commented on certain arguments made by the parties concerning whether Butamax could be irreparably harmed absent an injunction. (*Id.* at A26).

The district court found the parties to be "direct competitors in an emergent market." (*Id.* at A25.) The district court also acknowledged Gevo's evidence that Butamax "could be adequately compensated with monetary damages – since [Butamax] plans to pursue a licensing business model," but believed that Butamax's "business plan is not solely focused on licensing" and that it "intends to have two primary revenue streams." (*Id*. at A26 n.21.) [redacted]

[redacted]

[redacted]

Further, the district court stated generally that some reputational harm and the loss of a first mover advantage might accrue were Gevo to infringe, but made no findings on the balance of equities other than to map the positions of the parties.[9] (PI Order at A27.) The record below highlights the significantly different positions of the parties in the market – Gevo is a small start-up, (PI Tr. 353:11-354:17; 358:8-363:21, A16640-43), whereas Butamax is backed by two large, multi-national corporations.

[redacted]

[9] While Butamax argues that the district court subsequently made such a finding (BM Br. at 66), that decision was limited to the time period of an expedited appeal (*see generally* SQO, A16721-27), incorrectly interpreted Gevo's prior representations of its business plan (*Id.* at A16725) and has been stayed for its entire pendency by this Court. The district court's error in finding that [redacted] which this Court granted.

[redacted]

On the other hand, Butamax has immense resources and a guaranteed customer base because it is a joint venture between British Petroleum ("BP") and E.I. du Pont de Nemours ("DuPont"). (*See* PI Tr. 333:13-17, A16635.) Butamax comes to the table with the combined reputations of one of the largest oil companies in the world *combined* with one of the largest chemical companies in the world. (BM Release, A17389, A16857-59.)

Notwithstanding those resources, Butamax does not need to establish any substantial customer relationships. Its entire market could be built-in, as [redacted] Indeed, the district court found that Butamax's business plan was focused on this market. (PI Order at A25.)

[redacted] When it does go to market in 2014, Butamax plans to have a capacity of 900 million gallons per year, [redacted] (7/26/2012 Pr. Release, A16857.)

V. BUTAMAX'S VERSION OF THE FACTS RELIES ON WITNESSES THE DISTRICT COURT DISCREDITED AND OUT-OF-CONTEXT "ADMISSIONS"

Butamax's brief reads as if it had prevailed before the trial court: it presents only the direct testimony of its experts as the unblemished truth and takes alleged admissions of Gevo's witnesses completely out of context and without the benefit of the clarifications that the district court weighed.

Indeed, Butamax relies upon the direct testimony of Drs. Babbitt and Klibanov as if those witnesses were unimpeachable. (BM Br. at 11-21.) It neglects to mention that the district court ***twice*** rejected Dr. Klibanov's testimony. (PI Order at A21, A24 (disagreeing with Dr. Klibanov's testimony concerning claim construction and enablement).) Nor was this district court the first to find Dr. Klibanov's testimony not persuasive. *See, e.g.*, *Unigene Labs., Inc. v. Apotex*, 06-cv-5571, 2008 WL 3992294, at *8 (S.D.N.Y Aug. 28, 2008); *In re Omeprazole Patent Litig.*, 490 F. Supp. 2d 381, 463 (S.D.N.Y. 2007); *Novozymes A/S v.*

Genencor Int'l., Inc., 446 F. Supp. 2d 297, 328 (D. Del. 2006); *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 288 F. Supp. 2d 562, 579 (S.D.N.Y. 2003).

Further, the "admissions" of Gevo's witnesses relied upon by Butamax do not stand for the positions for which Butamax cites them:

- Dr. Stephanopoulos clarified that while there are potential circumstances in which modified yeast do not produce isobutanol, such as where he could intentionally knock out critical genes, there was "no reason to doubt" that the yeast cited would produce isobutanol. Dr. Stephanopoulos further explained that, with respect to Yocum, one of the references for anticipation, the only reasonable interpretation was that it produced *more* isobutanol than natural yeast. (Steph. Tr. at 305:20-306:1, A11403, A11420-21.)

- Dr. Stephanopoulos' statement in his textbook that metabolic maps, while useful, convey little information about the fluxes of energy through the pathways is irrelevant – Butamax claims a metabolic pathway set forth in its own metabolic map– but it is set forth in the prior art.

- Dr. Kirsch's suggestion that he would "want to knock out PDC" in 2012 – and every other statement cited by Butamax – is irrelevant to written description. A wish or an invitation to research is insufficient to show written description. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1356-57 (Fed. Cir. 2010) (en banc); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566-67 (Fed. Cir. 1997) (disclosure of what would make the claim obvious is insufficient).

- Dr. Kirsch's alleged admission that the specification did not "redefine" the term resulted from an out-of-left-field question, asked when he was not viewing the patent or his declaration. His subsequent testimony made plain that he understood the definition excluded NADH-dependent KARI enzymes. (PI Tr. 185:22-186:6, 187:5-25, A16562-63.)

SUMMARY OF THE ARGUMENT

This Court should affirm the district court's denial of Butamax's motion for preliminary injunction. A preliminary injunction is an extraordinary form of relief reserved only for plaintiffs who can demonstrate the four factors required for a preliminary injunction, including a likelihood of success at trial. After extensive submissions, live witnesses and video testimony, the district court concluded that Butamax likely "does not hold a valid patent, nor would [Gevo] infringe if it did."[10] In the district court's opinion, this was not a close call. In fact, when Butamax requested a temporary injunction pending this appeal, the district court was so underwhelmed by Butamax's infringement and validity arguments that it refused to hear them at oral argument and reaffirmed its conclusions in its decision.[11]

Against that background, Butamax asserts that the district court abused its wide discretion on multiple grounds because it did not accept the interpretations and conclusions of Butamax's experts. Nothing can be further from

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[10] (PI Order at A26.) As explained in Gevo's Reply In Support of Its Emergency Motion to Stay the Injunction Pending Appeal, "[t]he district court did not revise or reverse any of its invalidity and noninfringement findings, but nonetheless found that, [redacted], it should enjoin Gevo." (A17312; *see* A16897 at 12:9-14, A16902 at 30:22-30:24, A16723.)

[11] (A17045 at 12:1-14.)

the truth. The district court's opinion concerning Butamax's likelihood of success rests soundly on the intrinsic evidence presented before it and the testimony of the parties' fact and expert witnesses.

With respect to claim construction, the district court properly construed Butamax's claims to be limited to "solely NAD**P**H-dependent" KARI enzymes. The district court's ruling is based on the definition that Butamax instructed persons of skill to use in its patent.

With respect to infringement, Butamax did not meet its burden. Gevo presented evidence of the [redacted] In response, Butamax failed to present any evidence demonstrating that Gevo's KARI catalyzed NAD**P**H in the cell.

With respect to validity, Butamax also failed to meet its burden. The district court found that Butamax's patent was likely invalid for inherent anticipation. In doing so, the district court properly exercised its discretion to credit Gevo's witnesses over Dr. Klibanov.

The district court also found that the three references relied on by Butamax did not disclose the "PDC knockout" requirement of claim 13. This makes sense given that Butamax filed a new patent application — ***years*** after the original '889 application was filed — that claims this subject matter.

With respect to irreparable harm, the district court stated that this factor is "neutral" in the context of its overall analysis. Although the district court found Butamax and Gevo to be direct competitors, it did not weigh Butamax's licensing model. Butamax's desire to license its patents as one of its "two primary revenue streams" demonstrates that monetary damages are sufficient to remedy any harm to Butamax.

With respect to the balance of hardships, the differences between the parties tip the balance in Gevo's favor. Butamax is a joint venture between two industry titans. [redacted] do not pose any threat Butamax, which has a large built-in customer for its biobutanol product.

STANDARD OF REVIEW

"A preliminary injunction is a 'drastic and extraordinary remedy that is not to be routinely granted.'" *National Steel Car, Ltd. v. Canadian Pac. Ry., Ltd.*, 357 F.3d 1319, 1324 (Fed. Cir. 2004) (quoting *Intel Corp. v. ULSI Sys. Tech., Inc.*, 995 F.2d 1566, 1568 (Fed. Cir. 1993)).

On appeal of a preliminary injunction, this Court may reverse only if it finds a clear abuse of discretion by the district court. *See Abbott Labs., Inc. v. Sandoz, Inc.*, 566 F.3d 1282, 1298-99 (Fed. Cir. 2009) (setting forth standard and finding no abuse of discretion); *Altana Pharma AG v. Teva Pharms. USA, Inc.*, 566 F.3d 999, 1005 (Fed. Cir. 2009) (same).

Abuse of discretion may only be established by "showing that the court made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings." *See Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001) (quotation omitted). A district court's factual findings, both implicit and explicit, can be reversed only for clear error. *Id.* at 1358. In fact, when a trial judge's findings are based upon her "decision to credit the testimony of one of two or more witnesses," those findings "can virtually never be clear error." *Monon Corp. v. Stoughton Trailers Inc.*, 239 F.3d 1253, 1263-64 (Fed. Cir. 2001) (quoting *Anderson v. City of Bessemer City*, 470 U.S. 564, 575 (1985)); *see also New England Braiding Co., Inc. v. A.W. Chesterton Co.*, 970 F.2d 878, 882 (Fed. Cir. 1992) (explaining that a "credibility determination is well within the court's province when ruling on a preliminary motion" and that the Federal Circuit lacked any basis for overturning the district court's assessment).

Butamax's standard on appeal is even higher than this because an "appellant carries a heavier burden when seeking to reverse the denial of a preliminary injunction than seeking to reverse the grant of a preliminary injunction." *Altana Pharma*, 566 F.3d at 1005 (affirming a finding of substantial question of validity despite finding that the district court made a clear error in examining one of the prior art references). In such cases, the movant "must show

not only that one or more factors relied on by the district court was clearly erroneous, but also that a denial of the preliminary relief sought would amount to an abuse of the court's discretion upon reversal of an erroneous finding." *Id.* (quotation omitted).

ARGUMENT

I. THE DISTRICT COURT PROPERLY EXERCISED ITS DISCRETION IN FINDING GEVO LIKELY DOES NOT INFRINGE

Butamax's alleged "ordinary meaning" construction is simply untenable because it ignores the ***express definition*** of "acetohydroxy acid reductoisomerase" in the patent specification. The '889 patent specification states "[t]he following ***definitions*** and abbreviations ***are to be used*** for the interpretation of the claims and the specification." ('889 patent, 6:52-53 (emphasis added), A83.) The specification provides an explicit definition of the claim term at issue:

> The terms "acetohydroxy acid isomeroreductase" and "acetohydroxy acid reductoisomerase" ***are used interchangeably herein to refer to*** an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate using NADPH . . . as an electron donor.

(*Id.* at 7:8-13 (emphasis added), A84.) A patentee should not be permitted to claim the benefit of such a definition and then run away from that definition when it is convenient. *Ariad*, 598 F.3d at 1353-54 ("[T]he purpose of the written description requirement is to 'ensure that the scope of the right to exclude, as set forth in the

claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification." (quotations omitted).)

Based on the patentee's lexicography above, the district court construed "acetohydroxy acid isomeroreductase" to be solely NAD**P**H dependent. (*See* PI Order at A12.) In doing so, the district court compared that definition with a different definition used by the patentee, which unlike the claim term at issue, allowed the use of "***either*** NADH ***or*** NAD**P**H." (*Id*. at A12, A14.) Specifically, the district court concluded that because the other enzyme allowed either to be "us[ed]," the KARI enzyme in the patent's definition that mentioned only NAD**P**H must have some significance. (*See id*. at A14.) The district court also found support for its construction based on a comparison of *another* enzyme's definition that allowed the use of NAD**P**H ***and/or*** NADH. (*Id*. at A12.)

In the face of its unmistakable lexicography, Butamax maintains that the district court should apply the "ordinary and customary meaning," which it argues is "an enzyme structurally similar to known acetohydroxy acid reductoisomerase enzymes and that converts acetolactate (AL) to dihydroxy-isovalerate (DHIV)." (BM PI Rep. Br. at 5, A10303, A10311 ("Butamax did not redefine the meaning of [acetohydroxy acid reductoisomerase].").) On appeal, Butamax alleges that the district court erred by applying Butamax's own lexicography. (BM Br. at 37-40.)

Despite Butamax's assertion of error, there has rarely been a clearer case of lexicography. Not only does the term appear in an explicit definition section of the patent, it is offset in quotes and uses the word "herein" to make plain that this definition should be applied throughout the patent. ('889 patent, 7:8-13, A83.) These are the unmistakable trappings of lexicography. *See, e.g.*, *AstraZeneca AB v. Mut. Pharms. Co.*, 384 F.3d 1333, 1339-40 (Fed. Cir. 2004) (definitions section "provides a strong signal of lexicography"); *Sinorgchem Co. v. ITC*, 511 F.3d 1132, 1136 (Fed. Cir. 2007) (quotation marks and "is" (*i.e.*, "are") indicate clear lexicography).[12]

A. The District Court Applied The Correct Construction Consistent With The Definitions In The Specification And The Prosecution History

In finding that Gevo likely did not infringe, the district court applied the correct claim construction. In an effort to make the district court's construction appear controversial, Butamax misconstrues it. (BM Br. at 41-47). While the district court did opine that the enzyme was "***solely*** NAD**P**H dependent," it did so to explain that the reaction needed to be driven by that enzyme. (PI Order at A12.) It did not find the enzyme *never* would catalyze even a single reaction of NADH.

[12] Butamax's expert Dr. Babbitt admits that the KARI definition appears in the patent's "definitions section." (PI Tr. at 232:9-11, A16574.) She further agrees (continued...)

The district court recognized that dependency is different than a rare catalysis and construed the claim as "excluding an enzyme that is in any way NADH-dependent." (*Id.* A13.)

1. The Prosecution History Supports The District Court's Construction

The prosecution history is useful in interpreting the claims because it "provides evidence of how the PTO and the inventor understood the patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1317 (Fed. Cir. 2005). In addition, prosecution histories of related applications can be used to determine the meaning of the claims. *See Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004).

Here, the prosecution history confirms the district court's interpretation because it shows that not only did Butamax fail to discover NADH-dependent KARI enzymes until late 2008, but also that Butamax recognized the KARI's definition in the '889 patent ***did not cover*** NADH-dependent enzymes.

In 2008, three years after filing the '889 patent, Butamax filed a patent application representing that NADH-dependent KARI enzymes were an

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(...continued)

that the section created definitions of "a number of different terms." (PI Tr. at 228:23-229:1, A16573.)

advancement in the art. That application describes KARIs that "use NADH" as novel enzymes and mentions that the mutations allowed KARIs to "use NADH as opposed to NADPH." (*See* U.S. 12/337,736 at ¶¶ 6-9, 54, A6276, A6292, A6296.) The application also claims a method to change a KARI that "uses NAD**P**H" to one that "binds NADH." (*See id*. at claim 9, A6393 (emphasis added).) That application would have been superfluous if the '889 patent application covered such enzymes. *See Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 973 n.5 (Fed. Cir. 2006) ("If Kao had intended to claim salt forms of the copolymer in the '382 Patent, the subsequent patent application would have been superfluous."); *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1290, 1297 (Fed. Cir. 2009) (finding that the related application's inclusion of "Crystal B," absent from the patent at issue, suggests that the applicant intended to include only "Crystal A").

Further, the evidence demonstrates that well after Butamax applied for the '889 patent, it ***knew*** that patent was limited to NAD**P**H-dependent KARI enzymes. Specifically, in a December 2010 CIP application claiming priority to the '889 patent's original provisional application, Butamax ***changed the definition*** of the KARI enzyme to include the use of NAD**P**H ***or*** NADH and incorporated its NADH-dependent application by reference. (U.S. 12/966,333 at ¶¶ 55, 97, A8686, A8692, A8696-97.) If the term's definition, which required "using NADPH" as an electron donor could apply to either NAD**P**H or NADH-dependent enzymes, then

Butamax would have had no reason to redefine this term. Thus, Butamax ***itself*** understood its definition is limited to NAD**P**H-dependent enzymes, and having later determined how to manufacture NADH-dependent enzymes, it amended the KARI definition in a later patent. *See Phillips*, 415 F.3d at 1317 (observing that the prosecution history is useful to show how the patentee understood the claim term). This intrinsic evidence also makes it plain to one of ordinary skill in the art that the '889 patent covers only NAD**P**H-dependent enzymes.

2. Butamax's Claim Construction Leads With Litigation-Driven Extrinsic Evidence That Is Contradicted By The Intrinsic Evidence And Butamax's Pre-Litigation Actions

Butamax essentially builds its entire "ordinary meaning" argument using extrinsic evidence that it alleges is "undisputed." Its construction is based on the testimony of Drs. Babbitt and Klibanov – both of whom are litigation experts. (BM Br. at 37-38.) Butamax also relies upon an alleged admission from Dr. Kirsch. (BM Br. at 39.) Recognizing that Dr. Kirsch's testimony is being used out of context, the district court properly credited Dr. Kirsch's testimony that Gevo does not infringe the patent because it does not have the NAD**P**H-dependent KARI required by the '889 patent.[13] (PI Tr. at 185:22-187:25, A16562-63.)

[13] Neither the patent nor Dr. Kirsch's declaration was before Dr. Kirsch when he made the alleged admission. (PI Tr. at 183:6-185:25, A16562.)

Butamax's minor reliance on alleged intrinsic evidence is unpersuasive. (BM Br. at 43-45.) The fact that other references to a KARI do not explicitly mention NAD**P**H (*see* BM Br. at 43-44) is inapposite – the whole point of a definition is that it need not be repeated each time the term appears.

Butamax also points to a single enzyme mentioned in its patent that is allegedly a "preferred embodiment" with NADH-activity. (BM Br. at 42.) The NADH-activity is contradicted by Butamax's later patent application that stated that the "only ketol-acid reductoisomerase (KARI) enzymes known are those that bind NADPH . . . ." (U.S. 12/337,736 at ¶ 6, A6292.) Further, the enzyme is not a "preferred embodiment;" rather, it is mentioned as one of the "sequences [which] are available from a ***vast array of microorganisms***." ('889 patent at 7:14-16 (emphasis added).) In situations where there are many alleged preferred embodiments, the presumption that they should be included is a weak one. *See Sinorgchem*, 511 F.3d at 1138 (finding that excluding the disclosure of one of 21 "preferred embodiments" could not overcome the specification's lexicography).

Despite Butamax's attempt to create a claim differentiation argument, the district court correctly found no such differentiation was required:

> [W]hile [Butamax] suggests, based on the doctrine of claim differentiation, that the inclusion of claim 14 necessarily requires the KARI in claim 1 to be NADPH and/or NADH dependent (D.I. 195 at 5), the doctrine is rebuttable if "a contrary construction is dictated by the written description." *Regents of Univ. of Cal. v.*

> *Dakocytomation Cal., Inc.*, 517 F.3d 1364, 1375 (Fed. Cir. 2008). Moreover, because ***another enzyme*** in the five step process is explicitly defined as using NADPH and/or NADH, it is unnecessary to expand the term acetohydroxy acid isomeroreductase to include NADPH and NADH-dependent enzymes.

(PI Order at A14 (emphasis added).)

Further, Butamax's argument that Gevo has characterized its KARI as an EC number 1.1.1.86 (BM Br. at 34), is unconvincing; [redacted] In another misguided argument, Butamax alleges that the "ordinary meaning" of "acetohydroxy acid isomeroreductase enzyme" is undisputed, but cites only to the testimony and declarations of its experts. (BM Br. at 38.)

3. The Definitions Of The '889 Patent Require The KARI Enzyme To Be NADPH-Dependent

Butamax's "back-up" claim construction position is that "using NADPH" could infringe if the enzyme *even once* catalyzed the reaction with

NAD**P**H as an electron donor.[14] This construction would render the definitions in the specification completely meaningless. The KARI enzyme is defined as:

> The terms "acetohydroxy acid isomeroreductase" and "acetohydroxy acid reductoisomerase" are used interchangeably herein to refer to an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate ***using NADPH*** . . . ***as an electron donor.***

('889 patent, 7:8-13, A84 (emphasis added).) This definition, which is limited to using NAD**P**H, is in stark contrast to the other definitions in the specification, which allow the use of" ***either NADH or NADPH***" or "either NADH ***and/or*** NAD**P**H."

> The term "acylating aldehyde dehydrogenase" refers to an enzyme that catalyzes the conversion of isobutyryl-CoA to isobutyraldehyde, ***using either NADH or NADPH*** as electron donor.

[14] Indeed, Butamax's assertion seems to be that if an enzyme catalyzed NAD**P**H even *once* to make a single molecule of isobutanol, then all of the billions of other isobutanol molecules, that were ***not*** made with NAD**P**H, would also infringe, because an "additional" step would still be infringement. Each of these catalyses, however, would be outside the claims. While the term "comprising" does not preclude additional steps, neither does it reach into each of the claim terms and broaden them. *See, e.g.*, *Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337, 1343 (Fed. Cir. 2007) ("The presumption raised by the term 'comprising' does not reach into each of steps to render every word and phrase therein open-ended — especially where, as here, the patentee has narrowly defined the claim term it now seeks to have broadened."); *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1376 (Fed. Cir. 2005) ("'[c]omprising' is not a weasel word with which to abrogate claim limitations.")

(*Id.* at 8:17-20, A84 (emphasis added).) Butamax also identified enzymes that could use NADH ***and*** NAD**P**H:

> ["branched chain alcohol dehydrogenase"] enzymes utilize NADH (reduced nicotinamide adenine dinucleotide) ***and/or*** NAD**P**H as electron donor[s].

(*Id.* at 7:54-56 (emphasis added).)

Thus, where the patentee wanted to include NADH-dependent enzymes or those that use both cofactors, he clearly knew how to do so. If, as Butamax alleges, all KARIs "use" both NADH and NAD**P**H, then Butamax's selection of ***only one*** of the two must have ***some*** significance – the only reasonable interpretation is that "uses" NAD**P**H means "mostly catalyze by" NAD**P**H, *i.e.* NAD**P**H-dependent. The subsequent CIP application where Butamax changed the definition to include both NADH and NAD**P**H is also compelling evidence of the original limitation of its claims. (*See* U.S. 12/966,333 at ¶¶ 55, 97, A8692, A8696-97.) Where, as here, the patentee knew how to include two elements but did not do so, the claim should be construed to exclude the omitted element. *Abbott Labs.*, 566 F.3d at 1296-97 (construing the term "crystalline" to mean "Crystal A" because the patentee's use of "Crystal B" in a related application demonstrated its intent to limit the patent).

Butamax's claim construction arguments contradict its pre-litigation employment of the term "using NADH" and "using NAD**P**H," demonstrating that

these terms do not cover negligible catalysis. This contradiction is found in several places:

1. Butamax titled its subsequent patent application "Ketol-Acid Reductoisomerase ***Using NADH***."[15] (U.S. 12/337,736, A6276-6393 at A6276 (emphasis added).) If all KARIs have at least background activity with NADH and NAD**P**H, then Butamax's employment of "Using NADH" denotes that the KARI catalyzes mostly by NADH.[16]

2. In the same application, Butamax stated that "[t]he discovery of a KARI enzyme that ***can use*** NADH as a cofactor as opposed to NADPH would be an advance in the art." (*Id.* at ¶ 6, A6292; *see also* ¶ 2, A6292.) The method claim at issue claimed changing a KARI that "uses NAD**P**H" to a KARI that "binds NADH." (U.S. 12/337,736 at claim 9, A6393.) If, as Butamax alleges, all KARIs have at least background activity with both, then "***can use***" must signify some additional quantity, *i.e.*, the KARI is NADH-dependent; otherwise the language is meaningless because all KARIs could "use" NADH.

3. [redacted]

A similar conundrum is presented in claim 14, which states that one of the enzymes should "use NADH" (as the final enzyme already does). If even a single electron donation leads to "use," then this claim is ***entirely co-extensive*** with

[15] This application incorporated Butamax's CIP application by reference.

claim 1, because under Butamax's assertions, all of the enzymes "use" NADH. In other words, the "using NADH" limitation would not narrow claim 14 to distinguish it from claim 1. Butamax's own employment of the term "using NADH/NADPH" strongly suggests that the term means "solely NAD**P**H-dependent."

This definition is consistent with the everyday lexicon of "use" – a car ***uses*** gasoline as a fuel, not hydrogen, even if it combusts the occasional hydrogen atom. Similarly, if a lumberjack karate chops a tree with his hand but then cuts it down with a chainsaw, he ***used*** the chainsaw to cut down the tree, not his hand.

Further, if Butamax's construction were applied, then the definition covers all KARIs, even those invented after the filing date. Butamax's expert Dr. Babbitt, however, testified that the definition in the specification ***was different*** from today's formal definition of the term:

> Q. And so that would be a definition that's provided in the '889 patent following this statement that says that when interpreting these claims, you are to use these definitions; right?
>
> A. That's not how the enzyme listed there is defined formally.

(...continued)

[16] Indeed, this application employed "using NADH" synonymously with NADH-dependent enzymes. (*See id.* at ¶¶ 2, 54, 6, claim 9, A6292, A6296, A6393.)

(PI Tr. at 230:18-23, A16574.) Thus, Dr. Babbitt's testimony constitutes an admission that the '889 patent does not use the "ordinary meaning" sought by Butamax.

B. Butamax Did Not Carry Its Burden On Infringement Under Any Reasonable Claim Construction

Before the district court, Butamax failed to present any evidence that Gevo's KARI employed NAD**P**H ***inside*** the yeast cell. Gevo's KARI enzyme is highly advanced and was not even contemplated at the time of Butamax's invention. As Gevo's Drs. Glassner and Kirsch testified, [redacted] Thus, Gevo's KARI is clearly driven by NADH. The particulars of Gevo's process also militate against any NAD**P**H activity. As Dr. Glassner testified in his deposition and at the PI hearing, [redacted]

[redacted]

[redacted] Further, when the district court found that Gevo's KARI only might have "ancillary" NAD**P**H activity, it implicitly found that the studies relied on by Butamax did not reflect the conditions in the cell. (PI Order at A14.)

II. THE DISTRICT COURT PROPERLY EXERCISED ITS DISCRETION IN FINDING CLAIMS 1 AND 14 ARE LIKELY ANTICIPATED

A prior art reference which expressly or inherently contains each and every limitation of the claimed subject matter anticipates the claims. *Schering Corp. v. Geveva Pharms., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003). While possibilities are insufficient to show inherent disclosure, where the prior art shows that "the ***natural result flowing*** from the operation as taught" would result in the process of the claims, inherent anticipation is present. *King Pharms., Inc. v. Eon*

Labs, Inc., 616 F.3d 1267, 1275 (Fed. Cir. 2010) (quotation omitted and emphasis added).

A. The District Court Applied The Correct Legal Standard

Butamax alleges the district court legally erred by considering whether Gevo had raised a substantial question of validity — a standard it alleges is insufficient. This Court, however, applies the same standard. *See Sciele Pharma Inc. v. Lupin Ltd.*, 684 F.3d 1253, 1261 (Fed. Cir. 2012) ("We agree with Lupin that it has raised a substantial question of validity with respect to the '866 patent."); *Altana Pharma*, 566 F.3d at 1005-06.

Even the case relied upon by Butamax agrees that the substantial question test is a useful tool to determine whether a plaintiff showed likelihood of success on the merits and that, where the defendant has "presented an invalidity defense that the patentee has not shown lacks substantial merit, it necessarily follows" that the patentee has not shown a likelihood of success on the merits. *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1379-80 (Fed. Cir. 2009). Here, there is no question that the burden was met — the district court considered both sides of the evidence (PI Order at A17-19) and concluded that Gevo's defense did "not lack substantial merit" based upon the inherent isobutanol pathways disclosed in the art. (*Id*. at A22-23.) Indeed, the district court's actual conviction went further — it stated that "the court has concluded that [Butamax]

does not hold a valid patent, nor would [Gevo] infringe if it did" — a quote it repeated in a separate decision.[17] (*Id*. at A26; Status Quo Order at 3, A16723.)

B. Butamax's Assertions Of Error Misrepresent The District Court's Opinion, Rely Upon A Discredited Expert, And Misconstrue The Testimony Of Gevo's Witnesses

Butamax has failed to show that the district court abused its discretion in its factual findings regarding the inherent disclosure of the prior art. As explained above, the district court credited Dr. Stephanopoulos and the determination of the patent examiner. (PI Order at A22.) Dr. Stephanopoulos testified that the claims were inherently anticipated because the pathway claimed by Butamax was a natural pathway that, unless altered, operates in all yeast. Dr. Stephanopoulos further testified that, consistent with the remaining limitation of the claim 1, several prior art references modified one of the enzymes involved in the pathway. (PI Tr. at 121:12-19, 51:20-52:2, 59:15-60:3, 103:16-17, A16546, A16529, A16531, A16542.) Dr. Stephanopoulos also testified that claim 14 was anticipated because the last enzyme of the natural process — the alcohol

[17] In quotes like this one, the district court's independent judgment is manifest. As such, Butamax's allegation that the district court simply deferred to the examiner is wrong; the district court considered, and found persuasive the reasoning of the examiner, which is not improper. *See Kimberly-Clark Worldwide, Inc. v. First Baby Prods.*, 431 F. App'x 884, 889 n.3 (Fed. Cir. 2011) (finding reexamination rejection relevant to vulnerability of patent claims).

dehydrogenase enzyme — was naturally NADH-dependent. (PI Tr. at 80:25-81:8, A16536.) The district court's decision to credit Dr. Stephanopoulos on the factual issue of whether a reference inherently disclosed certain elements can "virtually never be clear error." *See Monon Corp. v. Stoughton Trailers, Inc.*, 239 F.3d 1253, 1263-64 (Fed. Cir. 2001) (citation omitted). Nor was it here.

1. Butamax's Assertions Of Technical Errors By The District Court Are Simply Untrue

Butamax alleges that the district court found anticipation of claim 14 based upon Larroy I and that the district court found invalidity based upon *express* anticipation. But even a cursory reading of the district court's opinion reveals that Butamax's contentions are without merit.

First, Butamax argues that "the district court erred in finding that claim 1 is expressly anticipated by a reference that undisputedly does not explicitly disclose every claim limitation." (BM Br. 53-54.) In fact, this is one of its primary bases for requesting reversal. (BM Br. at 2.) Contrary to Butamax's assertions, the district court found that one of the references, Larroy I, explicitly disclosed one limitation — "isobutanol production" — but found ***inherent*** anticipation based on Larroy I as well as other references. (PI Order at A22-23.) Indeed, the anticipation discussion of the district court's opinion dedicates almost the entire legal standard to inherency (*Id*. at A15-16), and mentions inherency in its

discussion of the arguments ***seven times***. (*Id*. at A18-19.) If there were any remaining doubt, the district court stated in a footnote that "[t]he court nevertheless concludes that its broad claim construction encompasses the ***inherent*** reactions . . . disclosed in the prior art references related to claim 14."[18] (*Id*. at A22 n.16 (emphasis added).)

Second, Butamax's allegation that the district court found anticipation of claim 14 based upon Larroy I is incorrect. Rather, the district court's opinion makes clear that it found that several references each independently anticipated the '889 patent; it referred to Larroy I as only one example of explicit "isobutanol production." (*See, e.g.*, *id*. at A22 ("[B]ecause the court does not construe the term 'engineered isobutanol pathway' to require that all enzymes in the pathway be engineered, and because the prior art ***references*** disclose genetically engineering one or more enzymes in the pathway, the court finds that [Gevo] has raised a substantial question regarding the ***validity of claims 1 and 14***.") (emphasis added).) Further, the court stated that, while "the parties spend little time discussing claim 14," it found that its claim construction encompassed the inherent reactions "disclosed by the prior art ***references*** related to claim 14." (*Id*. at A22 n.16 (emphasis added).)

[18] Butamax does not challenge this construction on appeal.

2. Dr. Stephanopoulos's Testimony Is Consistent With The District Court's Opinion

Butamax relies upon an out-of-context statement by Dr. Stephanopoulos that there are some conditions under which yeast do not produce isobutanol. (BM Br. at 55.) But as the district court properly found, Larroy I ***does*** disclose "isobutanol production," and maps the claimed pathway as contributing to that production. (PI Order at A22-23; Steph. Decl. ¶ 22, A9819; *see also* Stephanopoulos Ex. 14, Larroy I, A10087, A10094-95.) Further, Dr. Stephanopoulos testified with respect to one of these references, Yocum, that the only reasonable interpretation of the reference is that it ***increased*** isobutanol production because it enhanced one of the enzymes early in the isobutanol pathway. (Steph. Tr. at 305:20-306:1, A11420-21.) In any event, Dr. Stephanopoulos did not express doubt about whether any of the cited references would fail to produce isobutanol, but merely said that a person of ordinary skill could "cook-up" a yeast to "kill the pathway." (Steph. Tr. at 327:17-21, A11442.)

3. The District Court Did Not Abuse Its Discretion In Discrediting Dr. Klibanov's Testimony

Butamax's entire fact section regarding anticipation, and much of its argument section concerning the merits, is based upon the testimony of Dr. Klibanov. (BM Br. at 16-18, 55-56.) Butamax, however, neglects to mention that the district court ***twice*** rejected his testimony. (PI Order at A21, A24 n.18

(disagreeing with Dr. Klibanov's enablement testimony).) Butamax apparently believes it was unfair for the district court to discredit Dr. Klibanov based on his opinion that claim 1 of the '889 patent should be construed to require every step of the pathway to be engineered; but Butamax can cite only his ***inconsistent*** testimony suggesting the opposite. (*Compare* PI Tr. 291:20-24 *with* 302:6-9, A16625, A16628.) Dr. Klibanov's inconsistent testimony is not a basis to question the district court's findings, but a reason to affirm the district court. At a minimum, the district court did not abuse its discretion in determining which of the experts that testified before it were credible.

Moreover, the Derrick article Dr. Klibanov relied on was one that he admitted involved a limited carbon environment where the yeast did not produce ethanol, which is what yeast are ***best*** known for. (PI Tr. 294:1-4, A16626.) Thus, it is hardly surprising that the district court, or the many courts before it, did not credit Dr. Klibanov's testimony.

Dr. Klibanov's testimony, even if credited, does not defeat inherency. For inherency to be present, the claimed method must be "the ***natural result flowing*** from the operation as taught." *King Pharms.*, 616 F.3d at 1276. Starved yeast that do not produce ethanol are hardly a "natural result." Indeed, in *King,* the court found the prior art need not in every situation perform the claimed method. *Id.* ("[A] prior art product that sometimes, but not always, embodies a claimed

method nonetheless teaches that aspect of the invention") (quoting *Hewlett-Packard Co. v. Mustek Sys., Inc.*, 340 F.3d 1314, 1326 (Fed. Cir. 2003)).

Moreover, the assertion that the starved conditions could apply to the yeast in the references has no basis in the record. Indeed, every single one of the anticipatory references discloses a growth-friendly medium for the yeast. (U.S. 10/614,333 at A10191, A10214 ("In a preferred embodiment, a microorganism of the invention is cultured in media . . . comprising nutrients essential or beneficial to the maintenance and/or growth of the microorganism . . . ."); Elischweski, A10031, A10052 (growth friendly medium including glucose); Larroy I, A10087, A10089 ("grown in 2% yeast extract, 2% peptone and either 2% glucose, 2% glactose or 3% glycerol"); Bekkaoui, A9957 ("[C]ells were plated on . . . isoleucine and valine and glucose.").)[19]

III. THE DISTRICT COURT PROPERLY EXERCISED ITS DISCRETION IN FINDING CLAIM 13 IS LIKELY INVALID FOR FAILURE TO COMPLY WITH THE WRITTEN DESCRIPTION REQUIREMENT

The district court analyzed the substantial record provided by both parties in painstaking detail and recounted each paragraph relied upon by Butamax on appeal. (PI Order at A23-24.) Based on this analysis, the district court reached

two conclusions: (1) "there is no dispute that the specification of the '889 patent does not specifically describe the requirement of inactivated genes that reduce pyruvate decarboxylase activity"; and (2) that three citations provided by Butamax, including a citation to the Dickinson reference, did not satisfy the written description requirement. (*Id*.)

A. The District Court's Decision Is Supported By Substantial Undisputed Evidence That There Is No Written Description For Claim 13 In The Specification

To satisfy the written description requirement, the specification as filed must "clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (quotations omitted); *see also Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (a person of skill in the art must "immediately discern the limitation at issue in the claims" to satisfy written description) (citation omitted). Written description is separate from enablement and, as such, a disclosure that makes the invention obvious or invites a person of skill to conduct further research is insufficient. *See Ariad*, 598 F.3d at

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(...continued)

[19] Contrary to Butamax's nonobviousness arguments (BM Br. at 57-59), yeast have been used in the production of biofuels for years and isobutanol has been identified as a fuel of interest since the 1930s. (*See* A96633 at 18.) Both are relevant art.

1356-57; *Eli Lilly*, 119 F.3d at 1567 (disclosure that merely renders claimed invention obvious is insufficient for written description).

As conceded by Dr. Klibanov, there are no words in the specification of the '889 patent that identify inactivating genes that reduce PDC activity. (PI Tr. at 291:11, A16625.) Nor does any example or embodiment in the '889 patent contain a PDC deletion.

It is also undisputed that on April 16, 2011, Butamax made its first submission in the '889 patent that mentioned inactivating genes to reduce PDC activity, when it added claim 13. This was after Gevo published an application claiming PDC-knockouts in 2009. (*See* U.S. Pat. No. 8,017,375, A8514-18, A8550-51, 8661; *see also* Kirsch Decl. at ¶¶ 9, 13-14, A7211-13.) Similarly, it is undisputed that, after Gevo's publication, Butamax decided to file a CIP where it discussed PDC deletion for the first time. (*See* U.S. Pub. 2011/0313206A1, filed on December 13, 2010, A8686.) The reason for the deficiency in the '889 specification is plain – Butamax did not invent the PDC-inactivation technology of claim 13, and thus was not in possession of PDC-inactivation at the time the '889 patent was filed. *See Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) ("[O]ne cannot describe what one has not conceived.") (cited with approval in *Ariad*, 599 F.3d 1336).

Given that written description is a question of fact, *Ariad*, 598 F.3d at 1351, and this substantial history of undisputed evidence, it is difficult to imagine how the district court could have so "clearly erred" as to constitute an abuse of discretion.

B. Butamax's Expert Did Not Succeed In Finding An Adequate Description of Claim 13 In The Specification

Despite Butamax's admissions that the '889 patent does not specifically disclose limitations of claim 13, Butamax attempts to string together various unrelated parts of the specification to find written description support for claim 13. (BM Br. at 60-62.)

Specifically, to show "possession" of the PDC knockout, Butamax cites a portion of the '889 specification that is about another molecule. ('889 patent, 12:15-17, A7237.) Gevo's experts, Dr. Stephanopoulos and Dr. Kirsch, systematically proved that the citation is not about PDC, but another decarboxylase enzyme called KIVD. (*See* PI Tr. at 89:14-19, A16538.) Notably, Butamax's expert Dr. Klibanov agreed that the portion of the specification relied on by Butamax does not talk about inactivating a PDC gene. (*See* PI Tr. at 287:17, A16624.)

In yet another attempt to find written description support for claim 13, Butamax cites another portion of the '889 patent specification that does not

mention PDC activity. ('889 patent, 16:55-57, A88.) In testimony that the district court credited, Dr. Stephanopoulos testified that this passage was merely "a generic statement about eliminating competing pathways" that had "nothing to do with pyruvate carboxylase." (PI Tr. at 91:8-14, A16539.) Dr. Klibanov agreed that the citation does not discuss deleting PDC genes. (PI Tr. 289:1-3, A16624.)

Butamax's final attempt at written description support relies upon a citation of the Dickinson reference ***in the Background of the specification***. ('889 patent, 1:46-47, A81.) But, again as experts for both sides acknowledged, the Dickinson reference was not cited in context of gene inactivation in a PDC context but in the context of another enzyme in the Ehrlich pathway. (PI Tr. at 91:20-92:1, A16539; PI Tr. at 290:1, A16626.) The entire Background section provides zero discussion of PDC activity or gene inactivation.[20] ('889 patent, 1:20-67, A81.) Having examined each of these citations, the district court found that there was likely insufficient written description for claim 13. (PI Order at A23-24.)

[20] Dr. Kirsch's testimony that he would "want to" knock out PDC is irrelevant to written description. A vague suggestion of a general problem, with no specific suggestion of any solution, does not satisfy the written description requirement. *Ariad*, 598 F.3d at 1352-53.

C. The District Court Was Within Its Discretion To Find There Is A Substantial Question Of Validity With Respect To The Enablement Of Claim 13

Nor does "tossing out the mere germ of an idea . . . constitute an enabling disclosure." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). Recognizing this principle, the district court correctly dismissed the testimony of Dr. Klibanov that one of ordinary skill could make and use the invention without undue experimentation despite the absence of disclosure as to how to identify inactivating genes that reduce PDC activity. This is particularly true given the many inconsistent statements and damaging admissions on the record made by Dr. Klibanov. After carefully weighing the evidence and noting that the "parties' experts disagreed as to the extent of experimentation it would take to create the PDC-knockout isobutanol-producing yeast of claim 13," the district court found for Gevo. (PI Order at A24 n.18.)

Butamax's proposition that the district court "failed to consider . . . any of Butamax's evidence" is therefore incorrect. (BM Br. at 63.) The district court expressly considered both "parties' experts" and did not abuse its discretion in finding Gevo's experts more credible after having the opportunity to observe them during live testimony. (PI Order at A24 n.18.)

IV. BUTAMAX WILL NOT BE IRREPARABLY HARMED IN THE ABSENCE OF A PRELIMINARY INJUNCTION

While the district court found irreparable harm to Butamax if it had a valid and infringed patent, on the facts before it, the district court found that Butamax likely "does not hold a valid patent, nor would [Gevo] infringe if it did." (PI Order at A26.) Contrary to Butamax's mischaracterization of the district court's findings, the district court did not weigh this factor in favor of Butamax, but instead considered it to be "neutral" in the context of its analysis. (*Id*.)

Even if Butamax had a valid and infringed patent, after the Supreme Court's decision in *Ebay Inc. v. MercExchange, LLC,* no presumption of irreparable harm can be asserted absent a full and careful consideration of every part of the record. 547 U.S. 388, 393-94 (2006). Even though the district court found that Butamax and Gevo are head-to-head competitors, the record establishes that one of Butamax's "two primary revenue streams" is licensing. (PI Order at A26.) To establish irreparable harm, Butamax must show that monetary damages would be an insufficient remedy. *Altana Pharma AG v. Teva Pharms. USA, Inc.*, 532 F. Supp. 2d 666, 683 (D.N.J. 2007) ("[A] movant does not establish irreparable harm by arguing loss of revenue . . . where money damages are calculable and the defendants have the ability to pay any damages award."), *aff'd*, 566 F.3d 999 (Fed. Cir. 2009). Here, Butamax's reliance on an alleged loss of market share is an inadequate basis for irreparable harm because it can be

compensated by monetary damages. *Nutrition 21 v. U.S.*, 930 F.2d 867, 871 (Fed. Cir. 1991) ("[N]either the difficulty of calculating losses in market share, nor speculation that such losses might occur, amount to proof of special circumstances justifying the extraordinary relief of an injunction prior to trial") (citing *Nuclear–Chicago Corp. v. Nuclear Data, Inc.*, 465 F.2d 428 (7th Cir. 1972)).

Courts have repeatedly held that monetary damages are adequate to compensate for licensing activities. *See High Tech Med. Instrumentation, Inc. v. New Image Indus., Inc.*, 49 F.3d 1551, 1557 (Fed. Cir. 1995) (reversing district court's grant of a preliminary injunction because, among other reasons, the patentee's willingness to license its patent demonstrated it "is willing to forgo its patent rights for compensation"); *Ill. Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679, 683 (Fed. Cir. 1990) (endorsing district court's denial of a preliminary injunction where patent holder had licensed its patent because of the sufficiency of money damages).

Just as Butamax would set a royalty in its license agreements as part of its business model, should a trial later establish infringement of Butamax's patent by Gevo, Butamax can be adequately compensated by the district court awarding Butamax a reasonable royalty to make it whole for any lost licensing revenue.

V. THE BALANCE OF HARDSHIPS TIPS DECIDEDLY IN GEVO'S FAVOR

Even if irreparable harm were present, which it is not, the balance of hardships tips in Gevo's favor because: (1) Butamax will suffer little, if any, harm if Gevo is not enjoined and; (2) [redacted]

The district court devoted two full pages of its opinion to a discussion of irreparable harm. It, however, did not make findings on the balance of equities. The Supreme Court, in *Ebay*, challenged district courts not to simply adopt "expansive principles" or "general rule[s]" of injunctive relief, 547 U.S. 388, 393-94 (2006). Under *Ebay*, the equities weigh in favor of Gevo.

A. Butamax Will Suffer Little, If Any, Harm If Gevo Is Not Enjoined Prior To Trial

Although the district court cited harm to Butamax in the form of affected "reputation, goodwill, and business opportunities," (PI Order at A26), these considerations have substantially more effect on Gevo than Butamax. Butamax comes to the table with the reputation and financial backing of one of the largest oil companies in the world *combined* with one of the largest chemical companies in the world – BP and DuPont. Butamax has repeatedly traded on this seemingly inexhaustible reputation. (*See, e.g.*, Press Releases, A17389, A16857-59.)

[redacted]

In addition, Butamax's assertion that [redacted] prior to trial is once again belied by the situation. Indeed, [redacted] Butamax would have sufficient financial and reputational backing from its parent corporations and [redacted]

[21] Butamax's allegation that Gevo will harm the market itself by selling its product was not countenanced by the district court, (PI Order at A25 n.20), and is inconsistent with the idea that Gevo is seeding the market through testing contracts.

[redacted]

[redacted] Thus, any harm caused to Butamax by not enjoining Gevo would be minimal and readily remedied if Butamax were successful at trial.

B. Enjoining Gevo Would Irreparably Harm Gevo And [redacted]

[redacted] *See Bell & Howell Document Mgmt. Prods. Co. v. Altek Sys.*, 132 F.3d 701, 708 (Fed. Cir. 1997) (finding that the district court

properly considered that the larger corporation would be minimally affected, [redacted]

VI. THE PUBLIC INTEREST FAVORS GEVO

In the absence of a valid and infringed intellectual property right, the public interest favors competition. *St. Regis Paper Co. v. Royal Indus.*, 552 F.2d 309, 314 (9th Cir. 1977). Indeed, in the absence of a valid and infringed patent, the "public interest is best served by denying [a] preliminary injunction." *Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1348 (Fed. Cir. 2006).

Gevo's freedom to market benefits the public by providing a pioneering biofuel. [redacted] (*See* Schubert Tr. at 41:2-42:17, A6757, A6761.) Gevo is currently advancing the biofuels market and developing a new industry and job market within the United States. Preventing the public from obtaining an exciting renewable energy source and material based on a likely invalid patent that is likely not infringed should not be countenanced. *See E.I. duPont de Nemours & Co. v. Phillips Petroleum Co.*, 835 F.2d 277, 278 (Fed. Cir. 1987) (recognizing the public harm that may result from a shortage of polyethylene products absent a stay of injunction).

CONCLUSION

For the reasons set forth above, this Court should affirm the district court's denial of the preliminary injunction.

Dated: August 17, 2012

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I certify that this brief complies with the type-volume limitation specified in Federal Rule of Appellate Procedure 32(a)(7)(B). According to the word processing system used to prepare the brief, this brief contains 13907 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).

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CERTIFICATE OF SERVICE

I hereby certify that on August 17, 2102 two copies of the foregoing Non-confidential Opposition Brief for Defendant/Counterclaimant-Cross-Appellant Gevo, Inc., were served by email and first class U.S. Mail postage prepaid on the following counsel:

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